Title: Molecular dynamics simulations of the muscarinic receptor

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Abstract: This thesis is devoted to molecular dynamics simulations of the muscarinic M2 receptor placed in a phospholipidic membrane. Basic algorithms of molecular dynamics are described and applied on a simple model of rare gases. Relations for calculation of binding free energies are derived. Several tricks for saving up computational time are presented. Next part contains a brief description of proteins and cellular membranes, structure and biological relevance of muscarinic receptors and known crystal structures of the muscarinic M2 receptor.

The chapter with results contains detailed description of calculations of binding free energy differences for several ligands bound to the muscarinic M2 receptor. Obtained values match the experimental ones. Dynamics of the muscarinic M2 receptor was also studied yielding a direction for future studies of the activation mechanism. Short discussion on application of obtained results in rational drug design can be found in the Conclusion chapter.

Keywords: molecular dynamics, membrane proteins, free energy perturbation, muscarinic receptor, accelerated molecular dynamics